

Claims

1. A nucleic acid molecule which encodes a cell wall protein necessary for the hyphae development of a pathogenic fungal organism, selected from the group consisting of:

- a) a nucleic acid molecule having one of the nucleotide sequences shown in SEQ ID No. 1, SEQ ID No. 3 or SEQ ID No. 5,
- b) a nucleic acid molecule having a nucleotide sequence which encodes a protein having one of the amino acid sequences shown in SEQ ID No. 2, SEQ ID No. 4 or SEQ ID No. 6,
- c) a nucleic acid molecule having a nucleotide sequence which over its entire length shows a homology of at least 80% to a nucleotide sequence of one of the nucleic acid molecules of a) or b), and
- d) a nucleic acid molecule having a nucleotide sequence which is complementary to a nucleotide sequence of one of the nucleic acid molecules of a) to c).

2. The nucleic acid molecule as claimed in claim 1, the nucleic acid molecule having the sequence of the *RBR1* gene of *Candida albicans*.

3. The nucleic acid molecule as claimed in claim 1, the nucleic acid molecule having the sequence of the *RBR2* gene of *C. albicans*.

4. The nucleic acid molecule as claimed in claim 1, the nucleic acid molecule having the sequence of the *RBR3* gene of *C. albicans*.

5. The nucleic acid molecule as claimed in claim 2, the *RBR1* gene being a pH- and/or temperature-regulated gene.

6. The nucleic acid molecule as claimed in claim 2 or 5, the expression of the *RBR1* gene being activated by the repressor Nrg1p and repressed by the transcription factor Rim101p.

7. The nucleic acid molecule as claimed in one of claims 1 to 6, the nucleic acid molecule being present as a DNA, RNA, PNA or LNA molecule or as a mixed form thereof.

8. A fragment of a nucleic acid molecule as claimed in one of claims 1 to 7, **wherein** it can inhibit the expression

of a cell wall protein of a pathogenic fungal organism in antisense orientation to a promoter in a host cell and comprises at least 10 nucleotides.

9. The fragment as claimed in claim 8, **wherein** it comprises at least 15, in particular at least 25, preferably at least 50 and particularly preferably at least 100 nucleotides.

10. A vector, **which comprises** at least one nucleic acid molecule as claimed in one of claims 1 to 7 and/or at least one nucleic acid fragment as claimed in claim 8 or 9 under the functional control of at least one expression regulation element which guarantees the transcription of the nucleic acid into a translatable RNA and/or the translation of the RNA into a protein.

11. The vector as claimed in claim 10, **wherein** the vector is a plasmid, cosmid, bacteriophage or virus.

12. The vector as claimed in claimed 10 or 11, **wherein** the regulation element is a promoter, enhancer, silencer, 3'-transcription terminator or a ribosome binding site.

13. The vector as claimed in one of claims 10 to 12, the vector having a signal sequence for the transport of the

expressed protein into a cell organelle, a cell compartment, into the extracellular space or out of the cell.

14. The vector as claimed in one of claims 10 to 13, **wherein** the nucleic acid molecule or fragment thereof is arranged in an antisense orientation to the at least one regulation element.

15. A host cell, **wherein** it contains at least one vector as claimed in one of claims 10 to 14.

16. The host cell as claimed in claim 14, **wherein** the host cell is a prokaryotic or eukaryotic cell, **wherein** the host cell is a bacterial cell, yeast cell, insect cell or mammalian cell.

17. The host cell as claimed in claim 15 or 16.

18. The host cell as claimed in one of claims 15 to 17, **wherein** the host cell is a *C. albicans* cell.

19. The host cell as claimed in claim 18, **wherein** the *C. albicans* cell comprises a vector in which a nucleic acid molecule having one of the nucleotide sequences shown in SEQ ID No. 1, SEQ ID No. 3 or SEQ ID No. 5 or having a nucleotide sequence which encodes a protein having one of the amino acid

sequences shown in SEQ ID No. 2, SEQ ID No. 4 or SEQ ID No. 6 is arranged in antisense orientation to at least one regulation element.

20. A method for the production of a cell wall protein necessary for the hyphae development of a pathogenic fungal organism, in particular of the Rbr1p, Rbr2p or Rbr3p protein of *C. albicans*, comprising the culturing of a host cell as claimed in one of claims 15 to 18 in a suitable culture medium under conditions which allow the expression of the cell wall protein, and the obtainment of the expressed cell wall protein from the cell or from the medium.

21. A protein which has the amino acid sequence shown in SEQ ID No. 2 and which is encoded by the nucleic acid sequence shown in SEQ ID No. 1.

22. The protein as claimed in claim 21, the protein being the Rbr1p protein of *C. albicans*.

23. A protein which has the amino acid sequence shown in SEQ ID No. 4 and which is encoded by the nucleic acid sequence shown in SEQ ID No. 3.

24. The protein as claimed in claim 23, the protein being the Rbr2p protein of *C. albicans*.

25. A protein which has the amino acid sequence shown in SEQ ID No. 6 and which is encoded by the nucleic acid sequence shown in SEQ ID No. 5.

26. The protein as claimed in claim 25, the protein being the Rbr3p protein of *C. albicans*.

27. The protein as claimed in one of claims 21 to 26, produced by the method as claimed in claim 20.

28. An antibody which specifically recognizes a protein as claimed in one of claims 21 to 27 and binds thereto.

29. The antibody as claimed in claim 28, the antibody being a monoclonal or a polyclonal antibody.

30. An antibody which specifically recognizes an antibody as claimed in claim 28 or 29 and binds thereto.

31. A method for the characterization and/or for the detection of the hyphae stage of *Candida* cells or cells of pathogenic fungal organisms which are related to *Candida*, comprising the incubation of the cells or cell fractions thereof with an agent for the identification of the cell wall protein Rbr1p, Rbr2p and/or Rbr3p, of a homologous protein and/or of a fragment thereof, the detection of the protein or

of a fragment thereof indicating the presence of the virulent hyphae stage of the cells.

32. The method as claimed in claim 31, the *Candida* cells to be characterized being cells of *C. albicans*, *C. tropicalis*, *C. krusei*, *C. parapsilosis*, *C. guilliermondii*, *C. glabrata*, *C. dubliniensis* or *C. lusitaniae*.

33. The method as claimed in claim 31, the cells to be characterized being cells of pathogenic fungal organisms which are related to *Candida*, or cells of a *Trichosporon* species or of a *Blastoschizomyces* species.

34. The method as claimed in one of claims 31 to 33, the cells to be characterized being present in a biological sample.

35. The method as claimed in one of claims 31 to 33, the cells to be characterized being cells isolated from a biological sample and enriched intact cells.

36. The method as claimed in one of claims 31 to 33, isolated cell fractions being employed for the characterization which are obtainable by cell disruption and fractionation of *Candida* cells or cells of species related to *Candida* and comprise at least one cell wall fraction.

37. The method as claimed in one of claims 31 to 36, the agent employed for the identification of the protein Rbr1p, Rbr2p or Rbr3p, of a homologous protein thereof or of a fragment thereof being an immunological agent.

38. The method as claimed in claim 37, the immunological agent being an antiserum directed against the protein Rbr1p, Rbr2p or Rbr3p, an antibody as claimed in claim 28 or 29 directed against the protein Rbr1p, Rbr2p or Rbr3p or a fragment thereof or a complex thereof.

39. The method as claimed in claim 38, the antibody having a label selected from the group consisting of a dye label, a radiolabel, a fluorescent label, a chemiluminescent label or an enzyme inducing a measurable reaction.

40. A method for the detection of a *Candida* infection and/or of an infection by pathogenic organisms related to *Candida* in a biological sample obtained from a human or animal organism, the presence of the protein Rbr1p, Rbr2p and/or Rbr3p, of a homologous protein thereof and/or of a fragment thereof in the biological sample and/or in the cell wall of *Candida* cells or cells of pathogenic organisms related to *Candida* optionally contained in the biological sample being detected, comprising

- a) the incubation of the biological sample with an agent for the identification of the protein Rbr1p, Rbr2p and/or Rbr3p, a homologous protein thereof and/or a fragment thereof and
- b) the detection of the interaction of the identification means with the protein or fragment thereof.

41. The method as claimed in claim 40, the *Candida* cells being cells of *C. albicans*, *C. tropicalis*, *C. krusei*, *C. parapsilosis*, *C. guilliermondii*, *C. glabrata*, *C. dubliniensis* or *C. lusitaniae*.

42. The method as claimed in claim 40, the cells of pathogenic fungal organisms which are related to *Candida* being cells of a *Trichosporon* species or a *Blastoschizomyces* species.

43. The method as claimed in one of claims 40 to 42, the biological sample being a skin or mucous membrane swab, an organ biopsy, a tissue biopsy, a body fluid, a body secretion, stool or a rinse from cavities or hollow organs.

44. The method as claimed in claim 43, the body fluid being sputum, urine, pleural effusion, spinal fluid, lymph or blood.

45. The method as claimed in claim 44, the blood being present as an unpurified blood sample, blood plasma or blood serum.

46. The method as claimed in claim 44 or 45, invasive candidiasis being detected by the detection of the protein Rbr1p, Rbr2p or Rbr3p or of a fragment thereof in blood or in the cell wall of *Candida* cells contained in the blood.

47. The method as claimed in one of claims 40 to 46, the agent employed for the identification of the protein Rbr1p, Rbr2p or Rbr3p being an immunological agent.

48. The method as claimed in claim 47, the immunological agent being an antiserum directed against the protein Rbr1p, Rbr2p or Rbr3p, an antibody as claimed in claim 28 or 29 directed against the protein Rbr1p, Rbr2p or Rbr3p, or a fragment thereof or a complex thereof.

49. The method as claimed in claim 47 or 48, the antibody having a label selected from the group consisting of a dye label, a radiolabel, a fluorescent label, a chemiluminescent label or an enzyme inducing a measurable reaction.

50. A method for the discovery and identification of substances having therapeutic action against diseases which

are caused by *Candida* species or pathogenic fungal species which are related to *Candida*, a substance to be tested being brought into contact in a suitable medium with at least one agent selected from the group consisting of a nucleic acid molecule as claimed in one of claims 1 to 7, a nucleic acid fragment as claimed in claim 8 or 9, a vector as claimed in one of claims 10 to 14, a host cell as claimed in one of claims 15 to 19, a protein as claimed in one of claims 21 to 27 or an antibody as claimed in one of claims 28 to 30, and an interaction between the substance to be tested and the agent being detected.

51. A diagnostic composition comprising a nucleic acid molecule as claimed in one of claims 1 to 7, a nucleic acid fragment as claimed in claim 8 or 9, a vector as claimed in one of claims 10 to 14, a host cell as claimed in one of claims 15 to 19, a protein as claimed in one of claims 21 to 27 and/or an antibody as claimed in one of claims 28 to 30.

52. A pharmaceutical composition comprising a nucleic acid molecule as claimed in one of claims 1 to 7, a nucleic acid fragment as claimed in claim 8 or 9, a vector as claimed in one of claims 10 to 14, a host cell as claimed in one of claims 15 to 19, a protein as claimed in one of claims 21 to 27, an antibody as claimed in one of claims 28 to 30 and/or a

substance which was identified by means of the method as claimed in claim 50.

53. The pharmaceutical composition as claimed in claim 52, it being a vaccine which contains a protein as claimed in one of claims 21 to 27 and which is suitable for the active immunization of a human or animal body against a *Candida* infection.

54. The pharmaceutical composition as claimed in claim 52, it being a vaccine which contains an antibody as claimed in claim 28 or 29 and which is suitable for the passive immunization of a human or animal body against a *Candida* infection.

55. The pharmaceutical composition as claimed in claim 53 or 54, the vaccine being present as a lyophilizate.

56. The pharmaceutical composition as claimed in claim 53 or 54, the vaccine being present as an aqueous colloidal solution or suspension.

57. The pharmaceutical composition as claimed in one of claims 53 to 56, additionally containing at least one adjuvant.

58. A kit for the in vitro identification of the cell wall protein Rbr1p, Rbr2p and/or Rbr3p of *Candida* species or of a pathogenic organism related to *Candida* and/or for the in vitro detection of the virulence of *Candida* cells or of cells of an organism which is related to *Candida*, comprising at least one container having an antibody which specifically recognizes the protein Rbr1p, Rbr2p or Rbr3p or a fragment thereof and binds thereto.

59. The kit as claimed in claim 58, comprising a second container having the isolated and purified protein Rbr1p, Rbr2p and/or Rbr3p of *C. albicans*.

60. The use of a nucleic acid molecule as claimed in one of claims 1 to 7, of a nucleic acid fragment as claimed in claim 8 or 9, of a vector as claimed in one of claims 10 to 14, of a host cell as claimed in one of claims 15 to 19, of a protein as claimed in one of claims 21 to 27 or of an antibody as claimed in one of claims 28 to 30 for the diagnosis of diseases of a human or animal organism which are caused by *Candida* species or pathogenic fungal organisms which are related to *Candida*.

61. The use of a nucleic acid molecule as claimed in one of claims 1 to 7, of a nucleic acid fragment as claimed in claim 8 or 9, of a vector as claimed in one of claims 10 to

14, of a host cell as claimed in one of claims 15 to 19, of a protein as claimed in one of claims 21 to 27 or of an antibody as claimed in one of claims 28 to 30 for the production of a diagnostic composition for the diagnosis of diseases of a human or animal organism which are caused by *Candida* species or pathogenic fungal organisms which are related to *Candida*.

62. The use of an agent which decreases or inhibits the expression and/or activity of the cell wall protein Rbr1p, Rbr2p, Rbr3p and/or of a homologous protein thereof as an active compound for the treatment and/or prevention of diseases of a human or animal organism which are caused by *Candida* species or pathogenic fungal organisms which are related to *Candida*.

63. The use of an agent which decreases or inhibits the expression and/or activity of the cell wall protein Rbr1p, Rbr2p, Rbr3p and/or of a homologous protein thereof as an active compound for the production of a pharmaceutical composition for the treatment and/or prevention of diseases of a human or animal organism which are caused by *Candida* species or pathogenic fungal organisms which are related to *Candida*.

64. The use as claimed in claim 62 or 63, the agent being selected from the group consisting of a nucleic acid molecule as claimed in one of claims 1 to 7, a nucleic acid fragment as claimed in claim 8 or 9, a vector as claimed in one of claims 10 to 14, a host cell as claimed in one of claims 15 to 19, a protein as claimed in one of claims 21 to 27, an antibody as claimed in one of claims 28 to 30 or a substance which was identified by means of the method as claimed in claim 50.

65. The use of a nucleic acid molecule as claimed in one of claims 1 to 7, of a nucleic acid fragment as claimed in claim 8 or 9, of a vector as claimed in one of claims 10 to 14, of a host cell as claimed in one of claims 15 to 19, of a protein as claimed in one of claims 21 to 27 or of an antibody as claimed in one of claims 28 to 30 for the identification and/or for the detection of substances which inhibit the expression or activity of the Rbr1p protein in a pathogenic fungal organism and are suitable as an active compound for the production of a pharmaceutical composition for the control of complaints caused by *Candida* species.

66. The use of a nucleic acid molecule having one of the nucleotide sequences shown in SEQ ID No. 1, SEQ ID No. 3 or SEQ ID No. 5, of a nucleic acid molecule having a nucleotide sequence which encodes a protein having one of the amino acid

sequences shown in SEQ ID No. 2, SEQ ID No. 4 or SEQ ID No. 6, or of a fragment thereof for the isolation of a homologous nucleic acid which encodes the Rbr1p protein, the Rbr2p protein or Rbr3p protein of *C. tropicalis*, *C. krusei*, *C. parapsilosis*, *C. guilliermondii*, *C. glabrata*, *C. dubliniensis*, *C. lusitaniae*, of a *Trichosporon* species, of a *Blastoschizomyces* species or of another fungal pathogenic organism.

67. The use of an antibody as claimed in claim 28 or 29 for the characterization and/or for the detection of the virulent hyphae stage of *Candida* cells.